

Amendment and Response

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For: HEPATITIS C VIRUS HELICASE CRYSTALS, CRYSTALLOGRAPHIC STRUCTURE AND METHODS

Page 2 of 13

Please replace the paragraph beginning at page 16, line 24, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

a2 --The orthorhombic form of UHHO represents a conformational intermediate that is not easily modeled as a hinge, but appears as a conformation intermediate between the extreme positions of domain 2. The fact that the orthorhombic crystal form UHHO has an accessible NTP-binding site occupied by inorganic phosphate in the native crystal form suggests that it may be uniquely suited for the study of inhibitors or co-factors that bind at the NTP-binding site. This crystal form is also desirable in the study of cofactors because it grows from solutions that contain significant quantities of DMSO, which is often required to bring marginally soluble chemical entities into solution with HCV helicase.--

Please replace the paragraph beginning at page 24, line 5, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

a3 --For example, a system for reading a data storage medium may include a computer comprising a central processing unit ("CPU"), a working memory which may be, e.g., RAM (random access memory) or "core" memory, mass storage memory (such as one or more disk drives or CD-ROM drives), one or more display devices (e.g., cathode-ray tube ("CRT") displays, light emitting diode ("LED") displays, liquid crystal displays ("LCDs"), electroluminescent displays, vacuum fluorescent displays, field emission displays ("FEDs"), plasma displays, projection panels, etc.), one or more user input devices (e.g., keyboards, microphones, mice, touch screens, etc.), one or more input lines, and one or more output lines, all of which are interconnected by a conventional bidirectional system bus. The system may be a stand-alone computer, or may be networked (e.g., through local area networks, wide area networks, intranets, extranets, or the internet) to other systems (e.g., computers, hosts, servers, etc.). The system may also include additional computer controlled devices such as consumer electronics and appliances.--

Please replace the paragraph beginning at page 25, line 22, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

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--The structure coordinates set forth in Tables 1, 2, or 3 can be used to aid in obtaining structural information about another crystallized molecule or molecular complex. A "molecular complex" means a protein in covalent or non-covalent association with a chemical entity or compound. The method of the invention allows determination of at least a portion of the three-dimensional structure of molecules or molecular complexes which contain one or more structural features that are similar to structural features of Hepatitis C virus helicase. These molecules are referred to herein as "structurally homologous" to Hepatitis C virus helicase. Similar structural features can include, for example, regions of amino acid identity, conserved active site or binding site motifs, and similarly arranged secondary structural elements (e.g., α helices and β sheets) and the assembly of these elements into domains. Optionally, structural homology is determined by aligning the residues of the two amino acid sequences to optimize the number of identical amino acids along the lengths of their sequences; gaps in either or both sequences are permitted in making the alignment in order to optimize the number of identical amino acids, although the amino acids in each sequence must nonetheless remain in their proper order. Preferably, two amino acid sequences are compared using the Blastp program, version 2.0.9, of the BLAST 2 search algorithm, as described by Tatusova et al., *FEMS Microbiol Lett.*, 174:247-50 (1999), and available on the world wide web at ncbi.nlm.nih.gov/gorf/bl2.html. Preferably, the default values for all BLAST 2 search parameters are used, including matrix = BLOSUM62; open gap penalty = 11, extension gap penalty = 1, gap x_dropoff = 50, expect = 10, wordsize = 3, and filter on. In the comparison of two amino acid sequences using the BLAST search algorithm, structural similarity is referred to as "identity." Preferably, a structurally homologous molecule is a protein that has an amino acid sequence sharing at least 65% identity with the amino acid sequence of Hepatitis C virus helicase (SEQ ID NO: 1). More preferably, a protein that is structurally homologous to Hepatitis C virus helicase includes at least one contiguous stretch of at least 50 amino acids that shares at least 80% amino acid sequence identity with the